

IN THE CLAIMS (37 CFR 1.121 Revised)

1.- 2. (cancelled)

3.-15. (cancelled)

16. (withdrawn) A method of generating a pharmacophore model for the CYP2D6 inhibitory potency of selective serotonin reuptake inhibitor compounds comprising the steps of

(i) correlating the chemical features of the conformers of the compounds in a training set of selective serotonin reuptake inhibitor compounds with a set of two- and/or three-dimensional descriptors for the active site of the CYP2D6 enzyme; and

(ii) generating an equation relating the observed CYP2D6 inhibitory potency of said selective serotonin reuptake inhibitor compounds to a set of generated two- and/or three dimensional descriptors for the selective serotonin reuptake inhibitor compound.

17. (withdrawn) The method of claim 16 wherein the steps are carried out using the set of two- and/or three-dimensional descriptors for selective serotonin reuptake inhibitor compounds chosen from the 3D-QSAR functionality and the genetic function approximation equation of the CERIUS²™ software program.

18. (withdrawn) The method of claim 16 wherein the CYP2D6 inhibitory potency is a value determined by *in vitro* of the inhibition of the CYP2D6 enzyme reaction with bufuralol, said value selected from the group consisting of the IC₅₀ value, the % inhibition value or the K_i (apparent) value.

19. (withdrawn) The method of claim 16 wherein the CYP2D6 is native or recombinant CYP2D6.

20. (withdrawn) A method for determining the CYP2D6 inhibitory potency of an selective serotonin reuptake inhibitor compound comprising the steps of

(i) generating the two- and/or three-dimensional descriptors for said selective serotonin reuptake inhibitor compound;

(ii) inputting said three-dimensional descriptors into an equation relating the observed CYP2D6 inhibitory activity of a set of selective serotonin reuptake inhibitor compounds to a set of three-dimensional descriptors generated for those selective serotonin reuptake inhibitor compounds; and

(iii) solving said equation for the CYP2D6 inhibitory activity of the selective serotonin reuptake inhibitor compound corresponding to the generated three-dimensional descriptors of step (i).

21. (withdrawn) The method of claim 20 wherein steps (i) through (iii) are carried out using a software program.

22. (withdrawn) The method of claim 21 wherein the software program is the CERIOUS²™ program

23. (cancelled)

24. (withdrawn) A pharmacophore model for the CYP2D6 inhibitory potency of selective serotonin reuptake inhibitor compounds generated in accordance with the method of claim 16.

25. (currently amended) A pharmacophore model for the CYP2D6 inhibitory potency of selective serotonin reuptake inhibitor compounds ~~according to claim 23~~ generated by a method comprising the steps of

(i) generating a set of three-dimensional conformers for each of the compounds in a training set comprising five or more selective serotonin reuptake inhibitor compounds;

(ii) correlating each of the compounds of said training set with an observed value for CYP2D6 inhibitory potency;

(iii) generating from the conformers of step (i) a set of one or more pharmacophore test models, each said pharmacophore test model comprising 1 hydrogen bond acceptor, 1 hydrophobic feature and 1 hydrogen bond donor, arranged in three-dimensional space;

(iv) calculating the CYP2D6 inhibitory potency for each conformer generated in step (i) towards each of the pharmacophore test models generated in step (iii);

(v) calculating the total cost for each pharmacophore test model; and

(vi) choosing the lowest cost pharmacophore test model as the pharmacophore model;

wherein said steps are carried out with the molecular modeling software CATALST™.

26. (cancelled)

27. (withdrawn) A method for the identification of an selective serotonin reuptake inhibitor compound which does not possess significant inhibitory potency towards CYP2D6 comprising the steps of

- (i) generating two- and/or three-dimensional descriptors for an selective serotonin reuptake inhibitor compound;
- (ii) inputting said two- and/or three-dimensional descriptors for the selective serotonin reuptake inhibitor compound into the equation of claim 16;
- (iii) solving said equation for the inhibitory activity of the selective serotonin reuptake inhibitor compound corresponding to the generated two- and/or three-dimensional descriptors of step (i); and
- (iv) designating the compound as not being a significant inhibitor of CYP2D6 activity if the calculated $K_{i \text{ (apparent)}}$ value is greater than 1 μM .

28. (withdrawn) A method according to claim 27 where the calculated $K_{i \text{ (apparent)}}$ value is greater than 10 μM .

29. (withdrawn) A method according to claim 27 wherein the calculated $K_{i \text{ (apparent)}}$ value of step (iv) is greater than 100 μM .

30. (withdrawn) A selective serotonin reuptake inhibitor compound which does not possess significant inhibitory potency towards CYP2D6 identified by the method of claim 27.

31. (withdrawn) A pharmaceutical composition comprising an selective serotonin reuptake inhibitor compound, which does not possess significant inhibitory potency towards CYP2D6, according to claim 30.

32. (withdrawn) A method of treatment for a condition, disorder or disease for which an selective serotonin reuptake inhibitor compound is therapeutically useful comprising the administration of an selective serotonin reuptake inhibitor compound according to claim 30.

33. (withdrawn) A method according to claim 32 wherein the condition, disease or disorder is selected from the group consisting of nausea, asthma, migraine, arthritis, post-operative pain and depression.

34.-40. (cancelled)

41. (withdrawn) A computer-readable medium having stored thereon a pharmacophore model for selective serotonin reuptake inhibitor compounds which possess significant inhibitory potency towards CYP2D6 generated in accordance with the method of claim 16.

42. (withdrawn) A computer comprising a computer-readable medium according to claim 41.

43. (cancelled)